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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/077,817	09/14/1998	DANIEL CAPUT	IVD924	6529

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EXAMINER
BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 07/02/2002 28

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/077,817	Caput et al
Examiner	**Art Unit**
Nirmal S. Basi	1646

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 10, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *5-36, 38, and 44-114* is/are pending in the application.

4a) Of the above, claim(s) *5-36, 38, 52-71, and 89-110* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *44-51, 72-88, and 111-114* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☒ The proposed drawing correction filed on *4/10/02 & 10/25/00* is: a) ☒ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

1. Amendments filed 4/10/02 (paper number 27) has been entered. Applicant has added new claims 60-114. Claims 72-88, 111-114 as they pertain to the elected polypeptide of Group I (polypeptide of SEQ ID NO:2) will be examined. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 5-36, 38, 60-71, 89-110, are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action (7/18/00, paper number 1).

3. The proposed drawing correction and/or the proposed substitute sheets of drawings, filed on 4/10/02 have been approved. Formal Drawings are required. The Patent and Trademark Office no longer makes drawing changes (see prior Office Action). See 1017 O.G. 4. It is applicant's responsibility to ensure that the drawings are corrected.

4. ***Sequence Rules Compliance***

This application fails to comply with the sequence rules, 37 CFR 1.821-1.825. Nucleotide and polypeptide sequences must be identified with the corresponding SEQ ID NO. Title 37, Code of Federal Regulations, Section 1.821 states "reference must be made to the sequence by use of the assigned identifier", the identifier being SEQ ID NO. Sequences in Claims 111 must be identified by their corresponding SEQ ID NO:. Claim 111 refer to a

nucleotide sequence by Fig. without reference to a SEQ ID NO: identifier. Compliance with sequence rules is required.

Claim Rejection, 35 U.S.C. 112

5. Claims 72-88 and 1111-114 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim is 72, 83, 87 is indefinite because it is not clear what specific regions of the protein comprise a "biologically active fragment" and what activity is contained in said fragment. Further it is not clear if the fragments "having the ability to bind IL-13" infers that the fragments bind to IL-13 or merely have the potential to bind IL-13. It is suggested "having the ability to bind IL-13" be changed to "binds" to overcome the rejection. The recitation that an element is "having the ability to bind IL-13" or perform a function is not a positive limitation but only requires the ability to so perform. It does not constitute a limitation in any patentable sense. The metes and bounds of the claim are not clearly set forth.

Claim 78 is also indefinite because it is not clear the "(1)" refers to when recited in the phrase "(3) a nucleotide sequence capable of hybridizing under stringent conditions to (1)", I f applicant is referring to the nucleotide sequence in subsection (1) of the claim then it should be claimed accordingly.

Claim 78 and 111 are indefinite because it is unclear what is an "allelic variant", The term "variant" carries no weight in terms of structure and function and encompasses an

unlimited number of alterations and reads on unrelated molecules. Further "stringent conditions" are not specified. The metes and bounds of the group of sequences that would meet the limitations of the claim depend upon the precise conditions under which hybridizations were performed including wash conditions. Since the hybridization and wash conditions dictate which nucleic acid sequences remain specifically bound to the nucleic acid the metes and bounds of the claims cannot be determined without the disclosure of said conditions.

Claim 87 is indefinite because it is not clear what is the "mature sequence of Il-13" the "extracellular domain of sequence (1)" or intracellular domain of sequence (1)". Neither the SEQ ID NO: not the regions of the protein that comprise "mature sequence of Il-13" the "extracellular domain of sequence or intracellular domain are disclosed so as to allow the metes and bounds of the claim to be determined. Further it is not clear what is sequence (1). Sequences must be referred to by SEQ ID NO:.

Claim 111 is indefinite because it is not clear what sequence is being refereed to. Nucleotide sequences must be identified by SEQ ID NO:

Claims 73,77-82, 84-86, 88, 112-114 are indefinite because they depend on a indefinite base claim and fail to resolve the issues raised above.

6. The rejection of record of original claim 37, 48-51 under 35 U.S.C. 112, first paragraph is maintained. Newly added claims 74, 85, 88 are also rejected under 35 U.S.C. 112, first paragraph. The rejection of new claims 74, 85, 88 as it pertains to pharmaceutical is the same as that of record for claims 37 and 48-51. Applicant generally argues that the claimed

pharmaceutical compositions are useful in blocking the activity of IL-13. Applicants arguments have been fully considered but not found persuasive. The polypeptide of claimed invention has been stated in the specification as useful for blocking the activity of Il-13, IL-13 being a mediator of inflammatory mechanism, this does form a nexus to treatment of a specific disease. Applicant does not disclose the specific disease state that can be treated with claimed pharmaceutical but instead refers to general responses which are observed, e.g. modulate the immune response. What specific disease is treated with an antagonist of the claimed receptor of instant invention, for example? Applicant has only provide where the claimed protein is implicated.

7. Further claims 48-51, 74, 85, 88 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 48-51, 74, 85, 88 are rejected based on the failure of the specification to enable one of skill in the art to make and/or use the pharmaceutical composition encompassed by the claim. The pharmaceutical composition comprising the polypeptide set forth in SEQ ID NO:2 or fragments thereof infer a drug or medication with therapeutic activity. The specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claim without undue experimentation. Factors to be considered in determining whether undue

experimentation is required are summarized in In re Wands (8 USPQ2d 1400 (CA FC 1988)). The factors most relevant to this rejection are the scope of the claim, unpredictability in the art, the amount of experimentation required, and the amount of direction or guidance presented. The term "pharmaceutical" implies a treatment of a disease. Neither the specification nor the prior art provide sufficient guidance as to what specific diseases could be treated by administering a "pharmaceutical composition" comprising the claimed. Attempting to identify a disease treatable by such a "pharmaceutical composition" would constitute undue experimentation. Therefore one of skill in art would have to identify a disease treatable by said "pharmaceutical composition", determine effective compositions, determine effective doses to achieve the intended purpose, determine routes of effective administration, determine if the "pharmaceutical composition" can reach its target tissue without degradation and determine if it has a therapeutic effect, all of which would constitute undue experimentation Therefore, the unpredictability to achieve all the afore mentioned goals and the lack of guidance provided in the specification, the disclosure fails to enable one of skill in the art how to make and/or use the "pharmaceutical composition" encompassed by the claims. Amending the claims to a composition instead of "pharmaceutical composition would overcome Examiners rejection.

8. Claims 44, 46-51,72-81, 83-88 and 111-114 are newly rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for protein comprising SEQ ID NO:2, specific fragments of the protein of SEQ ID NO:2 which are of sufficient length to be used as epitopic portions of the polypeptide of SEQ ID NO:2, wherein said epitopic portions are useful

for producing antibodies which specifically bind to the protein of SEQ ID NO:2, specific fragments of the protein of SEQ ID NO:2 that bind interleukin-13, does not reasonably provide enablement for other proteins or protein The, specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to isolated protein that binds interleukin-13 or fragments thereof The specification discloses the protein of SEQ ID NO:2 and is shown to bind shown to bind Il-13. The critical feature of the isolated protein is that it binds IL-13, said critical feature is contained in a specific sequence of SEQ ID NO:2. The structure of SEQ ID NO:2 required for IL-13 binding has not been disclosed. The scope of the claims encompass other fragments that have not been specifically disclosed to have the critical feature of the invention, and further lack the elements that have been disclosed enabling. The specification does not identify any minimum size of fragments that would retain activity. Fragments, as written, embrace polynucleotide sequences which may be unrelated to the DNA encoding the protein of SEQ ID NO:20. Without disclosure of where specially, in the structure of the molecule, the critical feature is contained it accordingly follows that the specification does not adequately teach how to make or use a commensurate number of such species. One cannot make or use that which cannot be envisioned. Further using claimed protein, lacking the critical feature, for hybridization may lead to binding to nucleic acids which encode polypeptides unrelated to the protein of SEQ ID NO: 2. Applicant has not disclosed how to use said protein/fragments. Applicant has not

disclosed the gene encoding claimed protein or allelic variants. The disclosure does not teach how to make active fragments such fragments, or to use the numerous fragments which did not share one of the enabled functions set forth above e.g. for the production of an epitope fragment of protein of SEQ. ID. NO:2. Due to the large quantity of experimentation necessary to identify the DNA of instant invention containing the critical feature of the invention, the lack of direction/guidance presented in the specification regarding the identification, purification, isolation and characterization of said DNA, the unpredictability of the effects of mutation on the structure and function of proteins (since mutations of the DNA encoding the protein of SEQ ID NO:2 are also encompassed by the claim), and the breadth of the claim which fail to recite sufficient structural limitations, undue experimentation would be required of the skilled artisan to make or use the claimed invention in its full scope.

Further pertaining to claims 78, 87 and 1011, the instant fact pattern closely resembles that in Ex parte Maizel, 27 USPQ2d 1662 (BPAI 1992). In Ex parte Maizel, the claimed invention was directed to compounds which were defined in terms of function rather than sequence (i.e., "biologically functional equivalents"). The only disclosed compound in both the instant case and in Ex parte Maizel was the full length, naturally occurring protein. The Board found that there was no reasonable correlation between the scope of exclusive right desired by Appellant and the scope of enablement set forth in the patent application. Even though Appellant in Ex parte Maizel urged that the biologically functional equivalents would consist of proteins having amino acid substitutions wherein the substituted amino acids have similar hydrophobicity

and charge characteristics such that the substitutions are "conservative" and do not modify the basic functional equivalents of the protein, the Board found that the specification did not support such a definition, and that the claims encompassed an unduly broad number of compounds. Such is the instant situation. Clearly, a single disclosed sequence does not support claims to any protein derived from the same, given the lack of guidance regarding the structure of the nucleotide sequence encoding an interleukin-13 binding polypeptide.

9. Claims 44, 47, 48, and 51 remain rejected, new claims 72-74, 75-81, 83-88 and 101-114 newly are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed

The claims are drawn to isolated polypeptide comprising fragments of SEQ ID NO:2, polypeptide encoded by nucleotide sequences that hybridize to the nucleotide encoding the protein of SEQ ID NO:2, allelic variants.

Instant disclosure, nor prior art provide any data or suggest that the incomplete fragments of SEQ ID NO:2 have any biological activity. The instant disclosure of the distinct polypeptide of SEQ ID NO: ((380 amino acids) does not adequately describe the scope of the claimed genus, which encompasses a substantial variety of subgenera including full-length, truncated, fusion polypeptides and variants thereof; and pharmaceutical compositions comprising said polypeptides. A description of a genus of polypeptides may be achieved by means of a

recitation of a representative number of polypeptides, defined by an amino acid sequence, falling within the scope of the genus or of a recitation of structural and functional features common to members of the genus, which features constitute a substantial portion of the genus. *Regents of the University of California v. Eli Lilly & Co.*, 119 F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the claimed genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed or which sequences may be biologically active and what is that biological activity. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from others excluded are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed and predict their use. Further no identifying characteristic or property of the instant polypeptides is provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed.

The specification further fails to identify and describe the regulatory regions essential to the function of the claimed invention, which are required since the claimed invention currently encompasses the full length, truncated, fusion polypeptides and variants thereof. Since the disclosure fails to describe the common attributes or characteristics that identify members of the

genus, the disclosure of the ability to have any biological active sequence derived from SEQ ID NO:2, is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genus as broadly claimed. The allelic variants are not disclosed. The amino acids that comprise the specific domains is not disclosed.

An adequate written description of a protein, requires a precise definition, such as by structure, formula, chemical name, or physical properties, not a mere wish or plan for obtaining the claimed chemical invention. Accordingly, an adequate written description of a protein is more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the protein itself. Accordingly, the specification does not provide a written description of the scope claimed. Protein comprising specific fragments disclosed to bind interleukin 13 are enabled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who

has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

10. Claims 44, 45 and 47 remain rejected under 35 U.S.C. 102(b) as being anticipated by Vita et al. (reference B on PTO form 1449). Newly added claims 72, 73, 75, 77-84, 86-87 and 111 - 114 rejected under 35 U.S.C. 102(b) as being anticipated by Vita et al. Applicant argues vita does not disclose any amino acid sequences or the purified polypeptide of SEQ ID NO:2. Applicants arguments have been fully considered but not found persuasive. Examiner agrees Vita does not disclose the sequence of the protein in question. The claims required the invention be purified (claims 44-470 or isolated (claims 72, 73, 75, 77-84, 86-87 and 101 to 114). The protein of Vita is isolated, ie on a gel. The protein of Vita is purified, on a gel, although not to homogeneity. The claims only require isolated and purified protein and do not put a limitation on the extent of purification or isolation.

Vita et al. discloses IL-13 β receptor polypeptide purified from solubilized cells by electrophoresis (see for example Fig 4, panel B). Vita et al. do not disclose the sequence of said polypeptide, however, absent evidence to the contrary, it would be expected that the purified polypeptide disclosed by Vita et al. would inherently comprise the amino acid sequence of the polypeptide set forth in SEQ ID NO:2 or comprise fragments of SEQ ID NO:2. This is evidenced by the fact that the polypeptide disclosed by Vita et al. posses the same activity as the instant SEQ ID NO:2, with respect to IL-13 crosslinking, is from the same organism as the

instantly claimed polypeptide (human), and has an apparent molecule weight comparable to that disclosed in the instant specification (approximately 70kD).

No claim is allowed

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal Basi whose telephone number is (703) 308-9435. The examiner can normally be reached on Monday-Friday from 9:00 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for this Group is (703) 308-0294.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Nirmal S. Basi
Art Unit 1646
July 1, 2002

MICHAEL PAK
PRIMARY EXAMINER